> stomach), rhinitis (runny nose), rash and tachycardia (rapid heart beat). While dose-dependent, extra pyramidal symptoms typically occur at a rate that is comparable to that seen with placebo at doses less than or equal to 6 mg per day taken orally.

(emphasis added).

51. By signaling to investors in the September 4, 2001 press release that the Company stood ready to manufacture Risperdal Consta, defendants concealed the reasons for the August 1, 2001 Wilmington Facility Agreement and that the Wilmington facilities were in fact unable to begin commercial manufacture of the product at the expected levels.

52. Defendants' disclosure in September 4, 2001, of the fact that all antipsychotic medications have been associated with side effects was false and misleading. In raising such broad-based concerns about antipsychotic medications, including longer-acting injectable formulations of conventional antipsychotics, defendants sought to conceal the special safety concerns that would accompany the use of Risperdal when formulated using Medisorb technology for sustained release. To note these special safety concerns would have differentiated the Medisorb-based depot product on the basis of safety, dramatically increasing concerns about product marketability, particularly in special populations, as well as for safe use in treating behavioral and psychological symptoms detailed in the false and misleading Risk Assessment article. These concerns would also have contradicted defendants' claims of the "clear advantages" resulting from the application of Medisorb technology posted on defendants' Web site:

> ProLease® and Medisorb® Injectable Sustained-Release Drug Delivery Systems
>
> Alkermes® has developed two uniquely complementary platforms for drug delivery: ProLease and Medisorb injectable sustained-release technologies for both small and macromolecules. With release profiles lasting from days to months, each is designed to eliminate the need for frequent dosing. Each has the potential to:

- Improve patient compliance and convenience by reducing dosing frequency
- Improve safety and tolerability
- Reduce adverse effects associated with peak/trough levels of other (oral) dosage forms
- Commercialize products that would otherwise not be viable because of delivery or economic considerations
- Optimize product life cycle management

The advantages are clear.

53. On September 4, 2001, defendant Pops sold 7,812 Alkermes shares at $25.88 per share, and between October 24, 2001 and October 25, 2001, Pops sold 12,500 Alkermes shares at $25.01-$26.05 per share.

54. On September 4, 2001, defendant Landine sold 2,500 Alkermes shares at $25.88 per share, and between October 24, 2001 and October 25, 2001, Landine sold 4,000 Alkermes shares at $25.01-$26.05 per share.

55. Between September 4, 2001 and September 28, 2001, defendant Frates sold 4,000 Alkermes shares at $20.01-$25.88 per share and between October 3, 2001 and October 24, 2001, Frates sold 4,000 Alkermes shares at $20.53-$25.01 per share.

56. On September 4, 2001, defendant Breyer sold 7,500 Alkermes shares at $25.88 per share and between October 11, 2001 and October 25, 2001, Breyer sold 12,000 Alkermes shares at $22.67-$26.05 per share.

57. On October 30, 2001, the Company issued a press release entitled "Alkermes to Expand Production Facility to Meet Projected Demand for Long-Acting Formulation of Risperdal." The press release stated in part:

Alkermes, Inc. today announced the signing of an agreement with Janssen Pharmaceutical that provides for the expansion of Alkermes' manufacturing capacity for production of the new, long-acting injectable formulation of Risperdal® (risperidone). A new drug application (NDA) for the new formulation of Risperdal, currently the most widely prescribed antipsychotic medication in the United States, was submitted to the U.S. Food and Drug Administration on August 31, 2001. Risperdal is expected to be the first "atypical" antipsychotic to be available in a formulation that only requires administration every two weeks.

"Our current manufacturing facility is fully equipped to support launch quantities and to meet the early demand projected for long-acting Risperdal," stated David Broecker, Chief Operating Officer of Alkermes. "This expansion will include the construction of a separate, large-scale GMP facility on the same site and is designed to enable Alkermes to significantly expand our production capacity. Our agreement with Janssen eliminates the financial risk associated with the acceleration of this expansion."

Pursuant to the agreement announced today, Alkermes has committed to expand its production capacity prior to FDA approval of the new Risperdal formulation in exchange for certain guaranteed financial payments. In addition, Alkermes will receive, under earlier agreements, royalties and manufacturing payments from Janssen upon successful commercialization of the new, long-acting Risperdal.

The long-acting formulation of Risperdal uses Alkermes' proprietary, injectable sustained-release drug-delivery technology, Medisorb®. The technology is based on the encapsulation of drugs into small polymeric microspheres that degrade slowly and release the medication at a controlled rate following subcutaneous or intramuscular injection. Alkermes is developing Medisorb product candidates in collaboration with pharmaceutical and biotechnology companies and on its own.

58. Nearly three months had elapsed between the signing of the Wilmington Facility Agreement and defendants' announcement in the October 30, 2001 press release. Despite the claims in the press release regarding the ability of the Wilmington manufacturing facilities to produce launch quantities and meet the early demand projected for the Risperdal Consta once the FDA approved the NDA, defendants again concealed the fact that the only DMF in existence for the MTI facilities, established on March 15, 1990, was for the manufacture of Medisorb polymer

at the Blue Ash facility in Cincinnati, Ohio. No such document had ever been filed for the Wilmington, Ohio facilities for the production of Medisorb® injectable sustained-release drug delivery systems. Nor have defendants ever sustained a successful FDA pre-approval inspection in connection with the manufacture of commercial drug products in the Wilmington facilities. While a facilities DMF was not required under FDA regulations, the defendants were still required to produce and file one, by Janssen, under the 1997 Mfg. Agreement. Thus, despite assertions to the contrary in the October 30, 2001 press release, defendants remained wholly unable to begin commercial manufacture of the product at the expected levels.

59. The October 30, 2001 press release regarding the elimination of the financial risk associated with the Wilmington Facility Agreement was false and misleading since it failed to point out that: (I) the costs of the project are to be borne exclusively by the defendants, and not by Janssen, unless Janssen terminates the development program; (ii) after commercialization, the costs of the project come out of defendants' royalty revenue, unless sales of the product fall below some minimum revenue amount; and (iii) defendants separately and egregiously accounted for the royalties and manufacturing payments from Janssen in connection with sales of the product as an additional source of revenue, as if these payments were wholly unconnected with the terms of the Wilmington Facility Agreement.

60. Between November 1, 2001 and February 26, 2002, defendant Landine sold 16,000 Alkermes shares, defendant Frates sold 16,000 Alkermes shares, defendant Breyer sold 54,000 Alkermes shares and defendant Pops sold 50,000 Alkermes shares at prices between $24.23 and $28.27 per share.

61. On February 26, 2002, the Company issued a press release entitled "Poster Titled

'Maintenance of Efficacy Without Compromising Safety When Switching From Oral Risperidone to Risperdal Consta®, a Long-acting Injection Formulation of Risperidone' Posted on Alkermes' Web Site." The press release stated in part:

> Alkermes, Inc., today announced that it added a poster to its website entitled "Maintenance of Efficacy Without Compromising Safety When Switching from Oral Risperidone to Risperdal Consta®, a Long-acting Injection Formulation of Risperidone." The poster was presented today, Tuesday, February 26, 2002 at 12:30pm ET at the Winter Workshop on Schizophrenia in Davos, Switzerland. This poster demonstrates the maintenance of efficacy without compromising safety when switching from Risperdal® (risperidone) tablets to Risperdal Consta. The poster is available on the Alkermes website at www.alkermes.com/news.
>
> A new drug application (NDA) for Risperdal Consta was submitted to the U.S. Food and Drug Administration on August 31, 2001 by Johnson & Johnson Pharmaceutical Research & Development, which conducted the clinical-development program. If approved by the FDA, Risperdal Consta will be marketed in the United States by Janssen Pharmaceutical Products, LP and manufactured by Alkermes. Risperdal is currently the most widely prescribed antipsychotic medication in the United States and would be the first "atypical" antipsychotic to be available in a long-acting formulation. Risperdal Consta is a long-acting injectable formulation of Risperdal that uses Alkermes' proprietary, injectable sustained-release drug delivery technology, Medisorb®. The technology is based on the encapsulation of drugs into small polymeric microspheres that degrade slowly and release the medication at a controlled rate following subcutaneous or intramuscular injection. Alkermes is developing Medisorb product candidates in collaboration with pharmaceutical and biotechnology companies and on its own.

62. The defendants knew that the February 26, 2002 press release stating that the use of Risperdal Consta does not compromise patient safety was false and misleading because the Risperdal Consta dosage form cannot be removed once injected and there is no mechanism to discontinue delivery of the drug in patients once they are afflicted with adverse side effects, whether or not they had already used oral Risperdal.

63. On March 21, 2002, the Company issued a press release entitled "Alkermes and Reliant Pharmaceuticals Announce Merger." The press release stated in part:

Alkermes, Inc. and Reliant Pharmaceuticals, LLC ("Reliant") today announced that the Board of Directors of Alkermes and the Board of Managers of Reliant have each unanimously approved a definitive merger agreement between the two companies. The merger unites Reliant's three marketed product brands, product development pipeline, extensive U.S. sales and marketing infrastructure and management team with Alkermes' advanced drug formulation and development capabilities, pipeline of proprietary and partnered products and manufacturing capabilities to create a rapidly growing integrated pharmaceutical company.

The transaction is structured as a tax-free exchange of equity, in which non-Alkermes equity holders of Reliant will receive a total of 31.07 million shares of Alkermes stock or approximately 31% of the outstanding shares of the new company post-closing. Based upon the March 20, 2002 closing market price for Alkermes of $30.05 per share, the purchase price for the portion of Reliant not already owned by Alkermes is $934 million.

THE DEFENDANTS' SCHEME BEGINS TO UNRAVEL

64. On July 1, 2002, the Company issued a press release entitled "Alkermes Announces Receipt by Johnson & Johnson Pharmaceutical Research & Development of Non-Approvable Letter for Risperdal Consta." The press release stated in part:

Alkermes, Inc. today announced that Johnson & Johnson Pharmaceutical Research & Development, LLC has received a non-approvable letter from the U.S. Food and Drug Administration (FDA) related to its New Drug Application (NDA) for Risperdal Consta(TM) (risperidone) long-acting injection.

"One of the strengths of our business model is the quality of the pharmaceutical companies with whom we collaborate," said Richard Pops, Chief Executive Officer of Alkermes. "Johnson & Johnson is one of the world's leading health care companies. We have great confidence in relying on their ability and judgment in dealing with regulatory authorities around the world."

Risperdal Consta is a long-acting injectable formulation of Risperdal® that uses Alkermes' Medisorb® drug-delivery technology. If approved, Risperdal Consta will be manufactured by Alkermes and the product will be marketed by Janssen Pharmaceutical Products, L.P. in the United States, Janssen-Ortho in Canada and Janssen-Cilag elsewhere.

65. Similarly, on July 1, 2002, Alkermes' joint venture partner, Johnson & Johnson Pharmaceutical Research & Development, L.L.C., issued a press release entitled "Johnson & Johnson Pharmaceutical Research & Development, L.L.C., Receives Non-Approvable Letter for RISPERDAL® CONSTA™." The press release stated in part:

> Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD), today announced that it has received a non-approvable letter from the U.S. Food and Drug Administration (FDA) related to its New Drug Application (NDA) for RISPERDAL® CONSTA™ (risperidone) long-acting injection. Issued at the 10-month goal FDA has set for responding to standard NDAs, the letter invited further dialogue with the agency to resolve questions regarding certain aspects of the pre-clinical data. No significant concerns were raised regarding the manufacturing process.
>
> "We believe we will be able to satisfactorily resolve the FDA's questions about the pre-clinical data," said Harlan Weisman, M.D., executive vice president of research and development at J&JPRD. "We look forward to doing so in an expeditious manner and moving ahead with the approval process." RISPERDAL® CONSTA™ is a long-acting injectable formulation of RISPERDAL® that uses Alkermes' proprietary, injectable, extended-release, drug-delivery technology, Medisorb®. The technology is based on the encapsulation of drugs into small polymeric microspheres that degrade slowly and release the medication at a controlled rate following subcutaneous or intramuscular injection. If it is approved, RISPERDAL® CONSTA™ will be manufactured by Alkermes and marketed in the United States by Janssen Pharmaceutical Products, L.P.
>
> "We believe RISPERDAL® CONSTA™ will represent an important new treatment option for persons with schizophrenia by offering all of the benefits of an atypical antipsychotic in a long-acting form," Dr. Weisman continued. "It has been estimated that as few as 25 percent of persons with schizophrenia take their medication on a consistent basis – a problem that can lead to relapse and re-hospitalization. Because of its two-week duration of effect, thus eliminating the need for daily pills, RISPERDAL® CONSTA™ may help increase adherence to treatment."

66. Together, the disclosures of July 1, 2002, point to unresolved medical issues, such as those relating to safety and efficacy of the Risperdal Consta drug product. While the Johnson & Johnson disclosure indicated that there were no significant issues presented related to the

manufacturing process, defendants failed to note in their press release that they were still unable to begin commercial manufacture of the product for the U.S. markets at the expected levels. While at a very late stage of the NDA process, for a product that allegedly presented no significant issues regarding the manufacturing process itself, defendants were still at the earliest stage of refocusing their Wilmington research and development operations into an elaborate, highly automated commercial manufacturing facility, with plans to begin validation activities ***at the end of the third quarter 2002***. Thus, despite assurance of no significant manufacturing process issues in the July 1, 2002 Johnson & Johnson press release, the Wilmington facilities were in fact still wholly unable to begin commercial manufacture of the product for the U.S. markets at the expected levels.

67. As a result of defendants' announcement of the non-approvable letter for Risperdal Consta on July 1, 2002, Alkermes' stock price dropped precipitously over the two-day period following the announcement, from a high of $16.01 to a low of $4.04, or a drop of 74.8%, on total volume of 29 million shares.

POST CLASS PERIOD REVELATIONS

Failed Merger

68. On August 14, 2002, Reliant Pharmaceuticals terminated its merger agreement with Alkermes. While defendants had expected to consummate the transaction based on the overly inflated value of the Company's stock, they could not control the timing of the FDA's issuance of a rejection letter for Risperdal Consta.

Stroke and Death in the Elderly

69. On October 17, 2002, the Health Products and Food Branch of Health Canada

issued the following notice to healthcare professionals, titled "Updated Safety Information for Risperdal (Risperidone) in Elderly Dementia Patients, Announced in Canada":

> Further to discussions with Health Canada, Janssen-Ortho Inc. advised healthcare professionals of new safety information for the use of RISPERDAL (risperidone), an antipsychotic medication in elderly, dementia patients. The manufacturer has notified doctors and pharmacists of reports of strokes and stroke-like events in clinical studies in elderly patients with dementia taking RISPERDAL.
>
> Data were analyzed from four clinical studies in elderly, dementia patients. In two of these studies, a higher proportion of patients taking RISPERDAL experienced strokes or related events than did those who received placebo (sugar pill). Further information from ongoing analyses of clinical studies will be posted as it becomes available.
>
> Worldwide exposure to RISPERDAL in elderly, dementia patients is approximately 2.5 million patient years. From this patient population, there have been 37 reports of strokes or stroke-like events (1 in Canada), including 16 deaths (1 in Canada). Generally, there is an increased risk of strokes and stroke-like events in the elderly population.
>
> Patients or their caregivers should immediately report to their doctors any signs and symptoms of potential strokes such as sudden weakness or numbness in the face, arms or legs, and speech or vision problems. Patients or their caregivers should inform their doctors of their past and present medical history, including history of stroke or stroke-like events, and should also consult their doctor prior to making any changes in their medication.
>
> Information about this safety update has been sent to doctors and pharmacists to ensure that they are aware of this new safety information whenprescribing and dispensing RISPERDAL. The company is working with Health Canada to update the Canadian prescribing information for RISPERDAL. In the interim, all healthcare professionals are advised to review the healthcare professional letter.

70. The CVAE results of certain clinical studies cited by Health Canada were not discussed in the September 2000 Risk Assessment article or in the July 1, 2002, disclosures. Despite these omissions, the CVAEs of Risperdal were considered to be so serious that, once discovered by regulatory authorities, warnings were required by Canadian and U.S. authorities to

protect the health and welfare of elderly patients taking Risperdal. Defendants knew but concealed the fact that this warning would have a serious negative impact on the market for and approvability of Risperdal Consta because defendants knew it would be impossible to discontinue or withdraw, once administered, a deep intramuscular injection of the Risperdal Consta biweekly dosage form in the event that signs and symptoms of potential CVAEs were reported by elderly patients.

Tardive Dyskinesia

71. The Risk Assessment article of September 2000 also noted a single case of de novo tardive dyskinesia in a clinical study involving 413 patients. The August 9, 2002, U.K. product approval press release failed to note the potential for tardive dyskinesia side effects while using Risperdal Consta. A warning for tardive dyskinesia appearing on the U.S. package insert for oral and liquid dosage forms of Risperdal since 1999 provides a recommendation that withdrawal of the Risperdal drug therapy be considered should the symptoms of tardive dyskinesia appear. In such circumstances, the alternative use of Zyprexa or Clozaril has been reported. Tardive dyskinesia, a known Risperidone-induced side effect, is a syndrome marked by involuntary movement of the lips or jaw and certain other continuous muscle movements. Defendants knew but concealed the fact that if tardive dyskinesia was observed by a patient who was prescribed Risperdal Consta, it would be impossible for a healthcare provider to comply with the recommendation indicated on an approved U.S. package insert for current Risperdal dosage forms, to withdraw, once administered, a deep intramuscular injection of the Risperdal Consta biweekly dosage from patients afflicted with the drug-induced syndrome.

Extra pyramidal Symptoms

72. The defendants produced all clinical trial supplies used in clinical studies reported in the article entitled "The First Antipsychotic of the 2nd Generation in a Depot Form: Risperidone Microspheres in Intramuscular Injections," published in the Journal Psychiatric ("Psychiatric Paper") during the second half of 2002. The paper is summarized as follows:

> Summary
>
> Risperidone is the first antipsychotic of the 2nd generation that is distributed in depot injections. Intramuscular application leads to therapeutic plasma levels within 3-4 weeks – this is also the period for which risperidone has to be simultaneously administered perorally in the beginning of treatment. The depot injections reach steady-state plasma concentrations without major fluctuation or high peaks of maximum levels following the application.
>
> Risperidone in the depot form was tested in five 3-4 month trials, 3 of which were open and 2 double-blind, and in a single long-term, 50-week study, in which the total of 1892 patients treated for schizophrenic and schizoaffective disorders were involved. Risperidone depot injections were more effective than placebo and equally effective as the oral form of the same drug in influencing not only the positive, but also the negative and affective symptoms and in normalising the scores of the quality-of-life scale. 17.6 % of patients were rehospitalised during the one-year treatment and the length of inpatient treatment was significantly shorter.
>
> ***The most frequent side-effects included extra pyramidal reactions observed in 20-30 % of patients depending on the application dose,*** hyperprolactinemia, mild weight gain, and in 10-15 % of patients also headache, somnolence and dyspepsia.
>
> Risperidone in the depot form is a preferential choice for maintenance therapy of patients with schizophrenic and schizoaffective disorders who refuse oral administration of drugs or repeatedly discontinue therapy.

(emphasis added).

73. Extra pyramidal symptoms or EPS are characterized by stiffness, rigidity, uncontrollable tremors, involuntary movements, restlessness and other symptoms and are a

serious problem associated with antipsychotic medications. ***EPS are believed to have a major impact on patient compliance, especially for the majority of schizophrenia patients who are on long-term treatment.*** Defendants knew but concealed the fact that, paradoxically, the use of the Medisorb sustained-release delivery system with Risperdal ***almost doubles*** the occurrence of EPS, ***while actually making it impossible for afflicted patients to discontinue treatment***, since it would be impossible to discontinue or withdraw, once administered, a deep intramuscular injection of the Risperdal Consta biweekly dosage form in the event EPS arise.

74. The FDA-approved U.S. package insert indicates that EPS is an adverse event experienced with the use of Risperdal oral formulations. As many as 3.8% of patients treated with Risperdal discontinued use because of extra pyramidal symptoms in controlled clinical trials. Notably, the statement of the author of the Psychiatrie Paper actually belies the safety-based limitations on the marketability of Risperdal Consta by adopting a position that forces the use of the depot form of the drug on those patients who refuse Risperdal, ***when extra pyramidal symptoms would cause them to refuse Risperdal therapy:***

> Risperidone in the depot form is a preferential choice for maintenance therapy of patients with schizophrenic and schizoaffective disorders who refuse oral administration of drugs or repeatedly discontinue therapy.

75. The results reported in the Psychiatric Paper, of clinical studies necessary for product registration activities, point to the concealment by defendants during the Class Period of the facts relating to known clinical experience with Risperdal side effects that would have an exceptional impact on the marketability of the drug, **including *(I) whether or not Risperdal Consta can be safely given to patients absent prior patient experience with the drug; (ii) whether or not a period of safe use with oral formulations of Risperdal must be established***

prior to administration of Risperdal Consta; and (iii) whether or not these issues stood in the way of the successful achievement of defendants' product revenue and profitability goals.

76. The lowest ex-US dosage form of Risperdal Consta currently available, 25 mg, is equivalent to a 2 mg daily oral dosage. The FDA-approved U.S. package insert summarizes data demonstrating the dose-relatedness for the triggering of extra pyramidal symptoms associated with Risperdal treatment. Thus, a higher prescribed dose of Risperdal or an inadvertent acute overdose of Risperdal can trigger EPS. Defendants also knew, based on the FDA-approved U.S. package insert that the enzyme responsible for metabolism of risperidone to 9-hydroxyrisperidone hydroxyrisperidone is actually a family of polymorphic enzymes capable of wide variation in metabolic rates by race and that no definitive pharmacokinetic studies looking at differences in dosage requirements by race and gender have been performed for Risperdal. Defendants knew but concealed the fact that EPS would be an even more serious side effect for a depot form of Risperdal, by collaborating with its joint venture partner in the overseas marketing of the drug with the following warning in the event of "overdose," provided for in the U.K.-registered package insert for Risperdal Consta:

> Symptoms:
>
> > In general, reported signs and symptoms have been those resulting from an exaggeration of the drug's known pharmacological effects. These include drowsiness and sedation, tachycardia and hypotension, and extra pyramidal symptoms. In overdose, rare cases of QT-prolongation have been reported. In case of acute overdosage, the possibility of multiple drug involvement should be considered.
>
> Treatment:
>
> > Establish and maintain a clear airway, and ensure adequate oxygenation and ventilation. Cardiovascular monitoring should commence immediately and should

include continuous electrocardiographic monitoring to detect possible arrhythmias.

There is no specific antidote to Risperdal. Therefore appropriate supportive measures should be instituted. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents. In case of severe extra pyramidal symptoms, anticholinergic medication should be administered. Close medical supervision and monitoring should continue until the patient recovers.

Arrythmia and Sudden Death

77. Torsades de Pointes is a syndrome of polymorphic ventricular tachycardia – essentially, an excessively rapid heartbeat – occurring in the setting of marked prolongation of the electrocardiographic QT interval. It occurs in individuals genetically predisposed to the disorder and is a frequent cause of sudden death in these individuals. Defendants knew that adverse pro-arrhythmic effects linked to QT interval prolongation were of concern to the FDA and that as many as 40 marketed drugs, including Risperdal and a similar number of drugs under development have been found to prolong the QT interval. Drug induced Torsades de Pointes is a relatively rare event but can be as high as 2% to 3% with some drugs.

78. Defendants noted instances of tachycardia in their August 9, 2002, press release but failed to address how Risperdal Consta patients experiencing QT interval prolongation would be treated. Defendants were aware of the February 7, 2002, draft guidance titled "Safety Pharmacology Studies for Assessing the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals." This guidance concludes that, while recognizing that clinical data related to the measurement of QT interval prolongation is important, efforts must also focus on nonclinical and preclinical aspects predictive of the condition. Despite this knowledge, defendants concealed the fact that if QT interval prolongation would be

experienced by a patient who was prescribed Risperdal Consta, it would be impossible for a healthcare provider to discontinue treatment, since it is impossible to withdraw, once administered, a deep intramuscular injection of the Risperdal Consta biweekly dosage from patients afflicted with QT interval prolongation.

Drug-Drug Interactions

79. Drug-drug interactions are also an important safety concern. These interactions can occur when two or more drugs interact with each other. It is generally known that the need to administer selective serotonin[2] uptake inhibitors such as Zoloft or Prozac can slow the metabolism of Risperdal, resulting in Parkinson-like symptoms. Defendants concealed the fact that, in contrast to oral dosage forms, it would be impossible for a healthcare provider to immediately withdraw a deep intramuscular injection of the Risperdal Consta dosage form, even if the patient is faced with therapeutic needs and requirements incompatible with Risperdal therapy.

Diabetes: Risperdal Not An Exception

80. On Monday, August 25, 2003, Erica Goode, a human behavior staff writer for *The New York Times* ("NYT"), authored an article titled "3 Schizophrenia Drugs May Raise Diabetes Risk, Study Says" describing the risk of diabetes resulting from the use of Risperdal. The article stated in part:

> Three drugs commonly prescribed for schizophrenia and other psychotic illnesses increased patients' risk of developing diabetes when compared with older antipsychotic medications, researchers said yesterday, presenting the results from a long-awaited study of patients treated at veterans hospitals and clinics across the country.

---

[2] Serotonin is a neurotransmitter known to modulate mood, emotion, sleep and appetite and thus involved in the control of numerous behavioral and physiological functions.

The drugs – Zyprexa, made by Eli Lilly, Risperdal, made by Jannsen Pharmaceutica, and Seroquel, made by AstraZeneca – were associated with higher rates of diabetes than older generation drugs for schizophrenia like Haldol, the study found. But the increased risk was statistically significant only for Zyprexa and Risperdal, the researchers said, possibly because of the smaller number of subjects in the study who took Seroquel.

Younger patients, under age 54, who took Zyprexa or Risperdal showed the highest risk of developing diabetes, the study, led by Francesca Cunningham of the Department of Veterans Affairs at the University of Illinois at Chicago, found.

The results add to a growing number of reports linking Type 2 diabetes to some drugs in the class of antipsychotics known as atypicals.

"These findings are absolutely consistent with everything we've looked at and seen," said Robert Rosenheck, a professor of psychiatry and public health at Yale and an author of an earlier study that found an increased risk of diabetes with Zyprexa, Risperdal, Seroquel and Clozaril, made by Novartis.

Experts said the new findings underscored the need for patients who take the drugs and doctors who prescribe them to be alert for the symptoms of diabetes, including increased thirst, frequent urination, increased appetite or rapid weight gain.

Atypical antipsychotics, studies indicate, are less likely than older drugs to produce side effects like tardive dyskinesia, a devastating movement disorder. The newer drugs also appear more effective in preventing relapse in patients with schizophrenia and may be more effective in treating certain aspects of the illness.

More than 15 million prescriptions were written last year for Zyprexa and Risperdal, the two leading atypical antipsychotics, according to industry figures.

Researchers in the last two years have found higher rates of diabetes and hyperglycemia, medical conditions that are usually reversible, among patients taking the newer drugs. But many of the studies have been based on case reports in medical journals or filed voluntarily by doctors with the Food and Drug Administration, making it difficult to determine the size of the problem or whether it is associated with particular drugs or with the class of drugs as a whole.

The new study, scientists said, is important because of its careful methodology and substantial size: the researchers based their analyses on medical records from 19,878 veterans treated with an older or newer drug between October 1998 and October 2001.

> Of 5,981 veterans who took Zyprexa, 200, or 3.34 percent, developed diabetes, compared with 170, or 2.43 percent, of 7,009 veterans taking Haldol or another older medication. Of 5,901 patients taking Risperdal, 193, or 3.27 percent, developed diabetes; 21, or 2.39 percent, of 877 veterans taking Seroquel developed the illness. All three drugs raised a patient's chances of developing the illness by about 50 percent, but the meaning of the increased risk among patients taking Seroquel was unclear because of the smaller number of subjects who took the drug, the researchers said.
>
> "We need a larger number of observations to be certain what its risk is and whether it differs from other drugs," said Bruce Lambert, an associate professor of pharmacy administration at the University of Illinois at Chicago and an author of the study.
>
> The study was financed in part by Bristol Myers Squibb, the maker of Abilify, an atypical that had not entered the market when the study began and has not been systematically studied for a link to diabetes.
>
> * * *
>
> Laura Bradbard, a spokeswoman for the F.D.A., which has been tracking the diabetes issue, said the agency was reviewing the new findings, which were presented yesterday in Philadelphia at a meeting of the International Society for Pharmacoepidemiology ....
>
> The agency is considering whether to add or strengthen warnings in the labeling of certain drugs or on the class of drugs as a whole.
>
> How atypical antipsychotics might produce or uncover diabetes is unknown. Weight gain, a side effect of some drugs, may play a significant role, researchers believe. But P. Murali Doraiswamy, chief of the division of biological psychiatry at Duke University, said that in some cases the illness has come on rapidly, before patients have time to gain weight.

(emphasis added).

81. Despite earlier public assurances that Risperdal was found to be an exception to the increased risk of diabetes posed by certain atypical antipsychotics, defendants sought to conceal the serious negative impact on the market for and approvability of Risperdal Consta that would inevitably follow a link to diabetes.

82. The true facts, which were known by each of the defendants during the Class Period but were concealed from the investing public, were as follows:

(a) In an attempt to decrease development expenses and speed the product to market, defendants concealed the deficient nature of the manufacturing process for Medisorb PLGA polymer used to manufacture Risperdal Consta, resulting in quality management issues and delays in the development program.

(b) In order to conceal lot-to-lot variations resulting from the Medisorb polymer manufacturing process, defendants minimized process development and validation requirements, including the establishment of specifications and analytical tests necessary to control those variations.

(c) Significant quality issues for the manufacture of Risperdal Consta existed at the Wilmington, Ohio facilities, impacting the ability of the Company to meet clinical development timelines for Risperdal Consta.

(d) In order to avoid disclosure of the serious deficiencies of the Medisorb manufacturing process, particularly the lot-to-lot variation in molecular weight for Medisorb polymer, and in order to find a way to fix the desired molecular weight of the Risperdal Consta finished drug product, defendants patented a method to degrade the finished product to the desired molecular weight.

(e) Defendants' revenue projections for Risperdal Consta were grossly inflated based on defendants' concealment of the fact that Risperdal's adverse effects and safety or tolerability issues are worsened when Risperdal is formulated using Medisorb technology and used as intended.

(f) Defendants concealed the combined effect of the financial agreements reached with its joint venture partner, Janssen, that Risperdal Consta would not be profitable unless it achieved the high end of sales projections, an unlikely outcome because of the worsening of Risperdal's adverse effects and safety or tolerability issues when the drug was formulated using Medisorb technology and used as intended.

(g) The serious safety concerns for Risperdal "oral" and Risperdal Consta "depot" products, such as CVAEs in elderly patients, extra pyramidal symptoms, QT interval prolongation and diabetes, which were detected in clinical trials that went unreported to worldwide regulatory authorities for long periods, in some cases for studies completed well before the beginning of the Class Period, were negatively impacting the regulatory review process.

(h) For one or more reasons related to the known but unmet manufacturing, safety or efficacy requirements for the drug, the NDA for Risperdal Consta would not be approved on July 1, 2002.

(I) The failure to disclose the defective nature of the Risperdal Consta chemical and manufacturing controls, clinical program, safety and other issues preventing the Company from realizing product approval would prevent investors from learning the extent of the misrepresentations made to them during the Class Period.

FIRST CLAIM FOR RELIEF

For Violation of §10(b) of the 1934 Act and Rule 10b-5Against All Defendants

83. Plaintiff incorporates ¶¶1-82 by reference.

84. During the Class Period, defendants disseminated or approved the false statements